CLAIMS

What is claimed is:

1) A method for diagnosing a central nervous system disorder comprising measuring the level of NR2A and/or NR2B NMDA receptor or fragment thereof in a biological sample from a human subject, other than by measuring autoantibodies against a full sequence NR2A and/or NR2B receptor.

2) The method of claim 1 wherein the central nervous system disorder is TIA or stroke or the risk of TIA or stroke.

3) The method of claim 1 further comprising comparing the level of NR2A and/or NR2B NMDA receptor or fragment thereof in the biological sample to a baseline level selected from population norms and prior levels measured for the subject.

4) The method of claim 1 wherein the the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured directly from the level of the N-terminal domain of a NR2A and/or NR2B NMDA receptor or fragment thereof in the biological sample.

5) The method of claim 1 wherein the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured indirectly from the level of antibodies against the N-terminal domain of a NR2A and/or NR2B NMDA receptor, analogue thereof, or fragment thereof in the biological sample.

6) The method of claim 1 wherein the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured indirectly from the mRNA encoding the NR2A and/or NR2B NMDA receptor or fragment thereof in the biological sample.

7) The method of claim 1 wherein the the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured directly from the level of the peptide represented by SEQ ID NO:2, 3, 11, and/or 12.

8) The method of claim 1 wherein the the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured indirectly from the level of antibodies against a peptide of SEQ ID NO:2, 3, 11, and/or 12, analogue thereof, or fragment thereof, in the biological sample.

9) The method of claim 1 wherein the the level of NR2A and/or NR2B NMDA receptor or fragment thereof is measured indirectly from the level of cDNA corresponding to SEQ ID NOS: 5, 6, 7, 14, and/or 15, analogue thereof, or fragment thereof, in the biological sample.

10) The method of claim 1 for diagnosing the existence of TIA or stroke, further comprising withdrawing the biological sample from a human subject, wherein the biological sample is withdrawn within three hours of the onset of symptoms of TIA or stroke.

11) The method of claim 10 for diagnosing the existence of TIA or stroke, wherein the amount of time elapsed between withdrawing the biological sample from the subject, and detecting or measuring the presence or quantity of the NR2A and/or NR2B NMDA receptor or fragment thereof, is less than about one hour.

12) The method of claim 1 for diagnosing the existence of TIA or stroke further comprising, when the diagnosis confirms a stroke, evaluating from the level of NR2A and/or NR2B NMDA receptor or fragment thereof whether the stroke is ischemic or hemmorhagic and administering ischemic or hemmorhagic stroke therapy as appropriate.

13) The method of claim 1 for diagnosing the existence of TIA or stroke further comprising, if TIA and/or stroke is confirmed, evaluating from the level of NR2A and/or NR2B NMDA receptor or fragment thereof whether the episode is TIA or stroke and administering TIA or stroke therapy as appropriate.

14) The method of claim 1 for diagnosing the existence of TIA or stroke further comprising, if TIA and/or stroke is confirmed, evaluating from the level of NR2A and/or NR2B NMDA receptor or fragment thereof cranial infarct volume, and administering therapy consistent with the extent of cranial infarct.

15) The method of claim 1 wherein the NR2A and/or NR2B NMDA receptor or fragment thereof is measured by immunoassay.

16) The method of claim 1 wherein the NR2A and/or NR2B NMDA receptor or fragment thereof is detected or measured by agglutination comprising:

a) contacting the biological sample with poly- or monoclonal antibodies bound on an agglutinating carrier for sufficient time and under conditions to promote agglutination, wherein the antibodies are specific for the NR2A and/or NR2B NMDA receptor, analogue thereof, or fragment thereof; and

b) reading a signal generated from the agglutination; wherein the signal correlates to the titer of NR2A and/or NR2B NMDA receptor or fragment thereof present in the sample.

17) The method of claim 16, wherein the sufficient time period is 30 minutes or less.

18) The method of claim 16 wherein the carrier comprises polysterene latex beads having a mean diameter of from about 0.25 to about 0.4 μm.

19) The method of claim 1, wherein the biological sample is blood, urine, blood plasma, blood serum, cerebrospinal fluid, saliva, perspiration or brain tissue, or a derivative thereof.

20) The method of claim 1, wherein the biological sample is blood diluted to a ratio of from about 1:2 to about 1:32.

21) The method of claim 1, wherein levels of cDNA are measured by:

a) complexing the biological sample with one or more oligonucleotide primers to the cDNA for a sufficient time period and under conditions to promote amplification;

b) contacting the complex with an indicator reagent comprising a secondary oligonucleotide complementary to the cDNA attached to a signal-generating compound; and

c) measuring the signal.

22) The method of claim 21, wherein the signal-generating compound is selected from the group consisting of horseradish peroxidase, alkaline phosphatase, urinase and a non-enzymatic reagent.

23) The method of claim 21, wherein the cDNA comprises a poly- or oligonucleotide of SEQ ID NO:6 or 14, or a fragment thereof.

24) The method of claim 21, wherein the cDNA comprises a poly- or oligonucleotide of SEQ ID NO:7 or 15, or a fragment thereof.

25) The method of claim 21, wherein the one or more oligonucleotide primers are of SEQ ID NO:8, 9, 16, and/or 17.

26) The method of claim 1 wherein levels of NR2A and/or NR2B autoantibody are measured comprising:

a) contacting the biological sample with a protein fragment of the N-terminal domain of the NR2A and/or NR2B receptor for a time sufficient and under conditions to form a complx between autoantibodies in the sample and the protein fragment;

b) contacting the complex with an indicator reagent comprising a secondary antibody attached to a signal generating compound; and

c) measuring the signal.

27) The method of claim 26, wherein the secondary antibody is specific for the protein fragment.

28) The method of claim 26, wherein the secondary antibody is specific for the autoantibody being measured.

29) The method of claim 1, further comprising measuring one or more other biomarkers for TIA or stroke in the biological sample.

30) The method of claim 29 wherein the one or more biomarkers comprises an agonist or antagonist of an NMDA receptor.

31) The method of claim 29 wherein the one or more other biomarkers comprises glutamate or polyglutamate.

32) The method of claim 29 wherein the one or more other biomarkers comprises a thromboembolic biomarker.

33) The method of claim 29 wherein the one or more other biomarkers comprises homocysteine or polyhomocysteine and glutamate or polyglutamate.

34) The method of claim 1 further comprising, if the biological sample comprises a titer higher than 3.34 for glutamate, 2.23 for homocysteine and 2.63 for NR2A-B, administering TIA/stroke therapy or stroke risk reduction therapy.

35) The method of claim 1, further comprising, if the levels of NR2A cDNA in the subject are greater than about 1.0 pg/ml, administering TIA/stroke therapy or stroke risk reduction therapy.

36) The method of claim 1, further comprising, if the levels of NR2Aantibodies exceed 1.0 ng/ml, administering TIA/stroke therapy or stroke risk reduction therapy.

37) The method of claim 1 for diagnosing the risk of suffering TIA or stroke, in a subject not then exhibiting symptoms of TIA or stroke..

38) The method of claim 1 for diagnosing the progression of TIA or stroke further comprising measuring the level of NR2A and/or NR2B NMDA receptor or fragment thereof in a biological sample one or more additional times, at a frequency of less than about 6 hours.

39) The method of claim 38 wherein TIA or stroke therapy is concurrently being administered to the subject.

40) The method of claim 1 for diagnosing the remission of risk for stroke further comprising measuring the level of NR2A and/or NR2B NMDA receptor or fragment thereof in a biological sample one or more additional times, in a subject to whom stroke risk management therapy is administered.

41) A method for diagnosing a central nervous system disorder comprising directly or indirectly measuring:

a) the level of NR2A or NR2B NMDA receptor or fragment thereof in a subject; and

b) the level of one or more agonists or antagonists of the NR2A and/or NR2B receptor.

42) The method of claim 41 wherein the one or more agonists or antagonists comprise glutamate, polyglutamate, homocysteine and/or polyhomocysteine.

43) The method of claim 41 wherein the level of NR2A or NR2B NMDA receptor or fragment thereof in the subject is measured directly from the amount of NR2A or NR2B NMDA receptor or fragment thereof present in the biological sample.

44) The method of claim 41 wherein the level of NR2A or NR2B NMDA receptor or fragment thereof in a subject is measured indirectly from the amount of NR2A or NR2B NMDA receptor mRNA present in the biological sample.

45) The method of claim 41 wherein the level of NR2A or NR2B NMDA receptor or fragment thereof in the subject is measured from the amount of autobody against NR2A or NR2B NMDA receptor or fragment thereof in the biological sample.

46) A composition comprising a fragment of a polynucleic acid encoding the NR2A or NR2B subunit, wherein the fragment encodes the N-terminal domain of the NR2A or NR2B NMDA receptor.

47) A composition comprising an oligo- or polynucleotide selected from the group consisting of SEQ ID NO:6, 7, 8, 9, 15, 16, and 17, or a fragment thereof.

48) A protein fragment comprising the N-terminal domain of the NR2A or NR2B NMDA receptor.

49) A peptide or polypeptide of sequence listing SEQ ID NO: 2, 3, 4, 11, 12, or 13.

50) A test kit for detecting NR2A and/or NR2B cDNA amplification comprising:

a) NR2A and/or NR2B cDNA primer attached to a solid phase; and

b) an indicator reagent comprising a secondary oligonucleotide complementary to NR2A and/or NR2B cDNA, bound to a signal-generating compound capable of generating a measurable signal.

51) The test kit of claim 50, wherein the solid phase is a polymer matrix.

52) The test kit of claim 50, wherein the signal-generating compound is selected from the group consisting of horseradish peroxidase, alkaline phosphatase, urinase and non-enzymatic reagents.

53) A kit comprising:

a) poly- or monoclonal antibodies to NR2A and/or NR2B proteins immobilized on a carrier; and

b) a control solution.

54) The kit of claim 53 further comprising poly- or monoclonal antibodies to a second biomarker for a central nervous system disorder immobilized on a carrier.

55) The kit of claim 53 wherein the second biomarker comprises glutamate, polyglutamate, homocysteine, or polyhomocysteine.

56) The kit of claim 53 further comprising poly- or monoclonal antibodies to second and third biomarkers for a central nervous system disorder immobilized on carriers, wherein the second biomarker comprises glutamate or polyglutamate, and the third biomarker comprises homocysteine or polyhomocysteine.

57) A kit comprising:

a) protein fragments comprising the N-terminal domain of a NR2A and/or NR2B NMDA receptorpoly- or monoclonal antibodies immobilized on a carrier; and

b) an indicator reagent comprising a secondary antibody attached to a signal generating compound.

58) The kit of claim 57, wherein the secondary antibody is specific for the protein fragment.

59) The kit of claim 57, wherein the secondary antibody is specific for the autoantibody being measured.

60) A composition comprising a poly- or monoclonal antibodies against the NR2A or NR2B NMDA receptor or fragment thereof, covalently bound to latex beads.

61) The composition of claim 60 wherein the poly- or monoclonal antibodies are raised against the N-terminal domain of an NR2A or NR2B NMDA receptor or fragment thereof

62) The composition of claim 60 wherein the latex beads are polystyrene latex beads having a mean diameter of from about 0.25 to about 0.4 μm.